Exhibit 1

STAT+ [1]

Sesen Bio trial of cancer drug marked by misconduct and worrisome side effects, documents show

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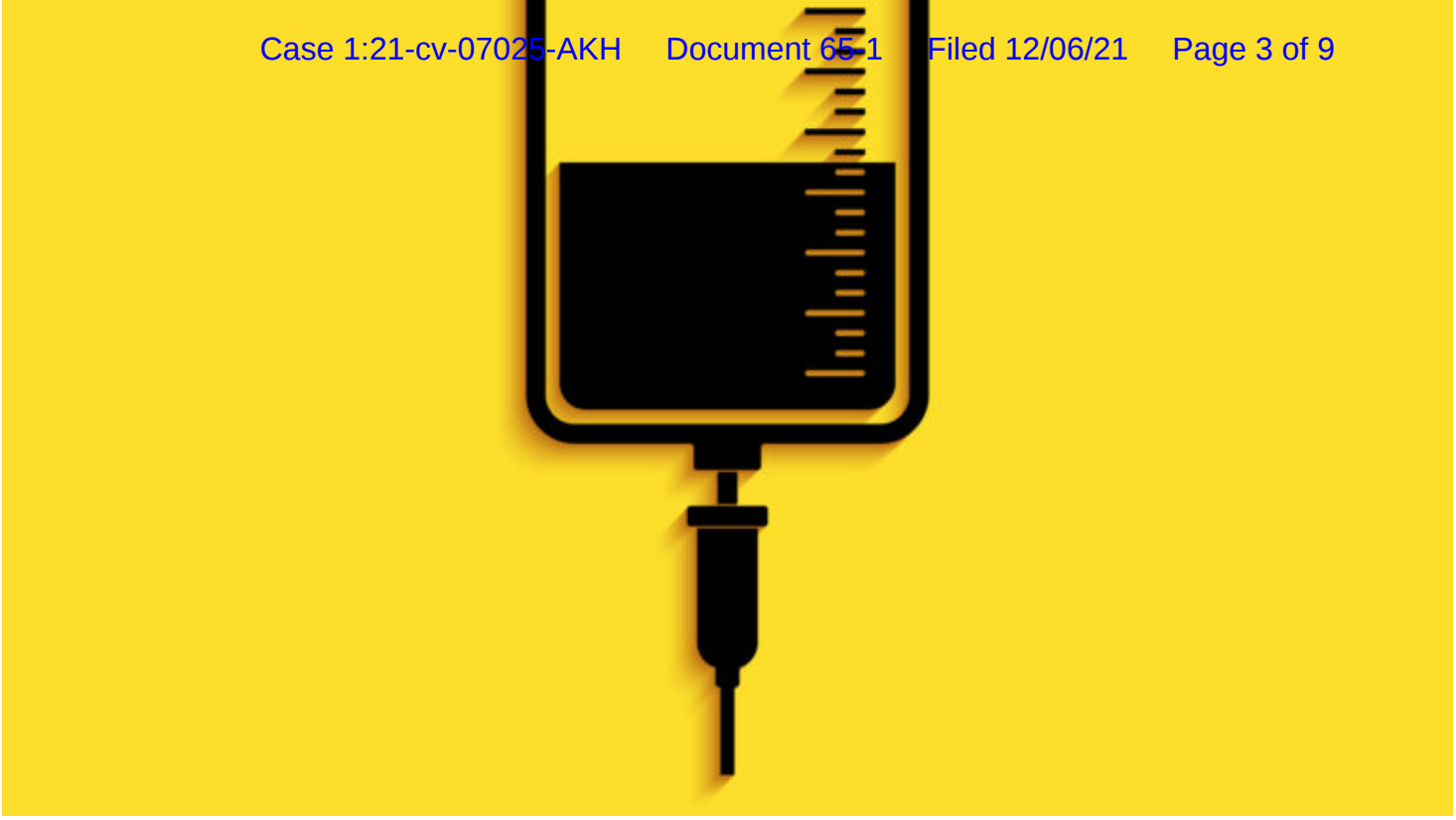
By Damian Garde[2] [3] Aug. 18, 2021



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The clinical trial of a cancer drug rejected by the Food and Drug Administration last week was marked by thousands of violations of study rules, damning investigator misconduct, and worrying signs of toxicity the company did not publicly disclose, according to hundreds of pages of internal documents obtained by STAT and confirmed by three people familiar with the matter.

Sesen Bio, a small biotech company that developed the bladder cancer drug, spent all of this year telling investors that its treatment was on its way to approval. After the FDA rejected it, CEO Thomas Cannell, fielding analyst questions on a Monday morning conference call, deemed it “a very surprising turn of events.”

But Sesen’s internal documents — which include safety reports, raw data, and communications between employees — suggest a seismic difference between the company’s public statements and the realities of the drug’s development. They also lift the curtain on revelations that might have played a role in the decision of regulators at the FDA, which, consistent with its practice in the case of rejected drugs, did not comment on its decision.

According to the documents, Sesen’s drug, called Vicineum, has led to dangerous elevations in liver enzymes that are associated with organ failure and death, which the

Cambridge, Mass., company did not mention in its filings with the Securities and Exchange Commission. The bladder cancer study, which enrolled about 130 patients, had more than 2,000 violations of trial protocol, including 215 classified as "major," according to company documents. The study's independent monitors reported three investigators to the FDA for particularly egregious violations, calling them issues of "serious noncompliance" that "placed subjects at risk of harm," according to the documents.

In 2016, one patient in the study was diagnosed with a drug-related case of liver failure and died within weeks, according to company documents. Two years later, presenting the study's results at a major urology conference, Sesen said there had been no drug-related deaths in the trial. Nine days after the presentation, Sesen raised $40 million in a stock offering.

"If this is true, there are serious issues that need to be addressed before this drug can even be considered for approval," said Ben Davies, a urologist at the University of Pittsburgh Medical Center who treats bladder cancer. "Most serious is this apparent liver toxicity," said Davies, who was not involved in Sesen's trial but reviewed documents at STAT's request.

In a statement to STAT provided a day before the rejection, Sesen did not deny the protocol violations, the investigator misconduct, or the omission of a drug-related death in its 2018 presentation. The company said Vicineum was not associated with life-threatening elevations in liver enzymes, a claim that contradicts multiple internal documents.

"We are confident that we have fully disclosed all relevant data to the FDA," Sesen said. "We stand by the safety and efficacy data of Vicineum," the company said, and as to the accuracy of its public statements, "we stand by the integrity of our disclosures and affirm they are based on the best information we have at the time."

An FDA spokesperson, provided a list of questions about Vicineum's safety and efficacy before the rejection, declined to comment, citing a policy that prohibits public statements about treatments undergoing review.

Sesen's stock price rose more than four-fold over the course of this year, buoyed by a series of positive press releases in which Sesen said the FDA had accepted its

application for approval and been supportive of Vicineum in multiple meetings. In recent months, Sesen said the FDA decided not to hold a public hearing for outside experts to go over the company's data, skipping a common step for new cancer treatments, and identified no problems in the company's supporting data. In June, Cannell described Vicineum[7] as "on a path to being a $1 billion to $3 billion drug."

On Monday, in an effort to explain Vicineum's rejection and the FDA's demand for a new study, Cannell cited the "tremendously heavy, really toxic media coverage" that followed the agency's June approval of Aduhelm, a treatment for Alzheimer's disease with debatable evidence of efficacy.

"When you're under pressure, the risk-averse or the safer strategy will always be to punt the ball down the field to ask for more data," Cannell said of the FDA's decision on Vicineum. Sesen expects to meet with the agency before the end of the year to discuss how the drug might one day win approval.

"I'm hopeful things will have calmed down by then," said Cannell, a veterinarian by training who joined Sesen from the bankrupted biotech firm Orexigen Therapeutics in 2018. "And I still think there are a lot of potential solutions."

Sesen, formerly known as Eleven Biotherapeutics and Viventia Bio, has been developing Vicineum for more than a decade. The drug is designed to work like a poison dart, pairing a bacterial toxin with a homing protein meant to latch onto cancerous cells, thereby killing tumors without harming healthy tissue. Because that toxin, produced by the bacterium Pseudomonas aeruginosa, can be deadly if it reaches the liver, Vicineum has to be administered directly to the site of the cancer.

But data from Sesen's clinical trials suggested Vicineum was leaking out into the body, leading to worrisome side effects, according to internal company documents. In clinical trials testing Vicineum against head and neck cancer, one patient died of liver failure, according to the documents, and another matched the criteria for a clinical rule of thumb called Hy's Law, meaning a patient is at serious risk for fatal, drug-induced liver injury. That risk is particularly serious in the eyes of the FDA, and it's the most common reason drugs are pulled from the market over safety, according to an agency guidance[8].

A similar pattern emerged in Sesen's Phase 3 bladder cancer study, called VISTA. One patient met the criteria for Hy's Law, suggesting Vicineum led to serious liver toxicity, according to the documents. Another patient was diagnosed with life-threatening, drug-induced liver failure, confirmed by biopsy, according to the documents.

In its statement, Sesen said the company "thoroughly reviewed" data from VISTA and "confirmed there were no cases of Hy's Law based on the clinical criteria as stipulated by FDA guidance." In the head and neck cancer study, "the data showed some elevated liver enzymes that have not been determined to be cases of Hy's Law," Sesen said. Both claims are contradicted by company documents, including a clinical report concluding one patient "met the criteria for Hy's Law" and internal communications about a second patient in which one employee wrote "I agree this is a Hy's Law case."

VISTA was also plagued by serious investigator misconduct that threatened the integrity of the data, according to documents. In 2017 and 2018, Copernicus, a firm Sesen hired to monitor its trial, found three doctors in the study were guilty of "serious noncompliance," "continued noncompliance," and actions that "placed subjects at risk of harm," according to reports sent to the FDA.

Separately, one investigator had his clinic closed in 2017 after his hospital's disciplinary committee concluded[9] he had engaged in "disgraceful, dishonorable, or unprofessional" behavior. A second investigator was found to be back-dating data, according to internal Sesen documents, casting serious doubt on any information gathered from his clinic. In each case, the company was advised that "the data from these affected centers cannot be used in any data analysis" submitted to the FDA, according to the documents. Despite that, Sesen included results from both sites in its application for Vicineum's approval, according to the documents.

In its statement, Sesen did not deny any instances of investigator misconduct in VISTA and did not dispute that it submitted tainted data to the FDA. "We are confident that we have fully disclosed all relevant data to the FDA," the company said, adding that "great care was taken every step of the way to ensure patient safety."

By 2018, Sesen had gathered enough data from VISTA to present preliminary results. On May 21, 2018, at the annual meeting of the American Urological Association, Sesen told attendees of the plenary session that Vicineum demonstrated a positive

response rate and that, as of April 2018, there had been no drug-related deaths[11] in the study.

That wasn't true. Two years before, a patient in VISTA died of liver failure that doctors determined was caused by Vicineum, according to company documents. That fact is reflected in Sesen's more recent descriptions of VISTA's trial results, but it was missing from the company's American Urological Association presentation, and it was nowhere to be found in a 46-page prospectus[12], filed with the SEC on May 30, 2018. Sesen used that document, which claimed there were "no [fatal] treatment-related adverse events," to raise $40 million from investors[13].

In its statement, Sesen did not dispute the timing of the patient's death or the absence of that information from its presentation and prospectus. "For each disclosure, which was also shared with the FDA per regulations, we included the best information we had at the time based on the preliminary results and the investigator's evolving perspective," the company said.

Over the ensuing years, Sesen's public statements suggested Vicineum was on a smooth path to approval. In late 2020[14], the company submitted its FDA application, accompanying the news with a statement from Cannell that "our strong non-clinical and clinical data … give us confidence in the regulatory path forward." In February[15], when the FDA granted Vicineum a priority review and opted against holding a public hearing on the drug, Cannell said "with these critical FDA decisions, we have reached an inflection point for the company." In July[16], Cannell said the company was "very pleased with the outcome" of a recent meeting with the agency and continued "to feel encouraged by the level of engagement from the FDA in our ongoing discussions regarding" Vicineum's approval.

The agency promised to render a decision on Vicineum by Aug. 18, Sesen said. By Aug. 13, Sesen's stock price hit a 52-week high of $6.04 on investors' expectation of FDA approval. That afternoon, Sesen halted trading to disclose Vicineum's rejection. When trading resumed, the company was worth about 90 cents per share.

The Vicineum saga underlines a longstanding frustration for investors in small, publicly traded biotech companies. The FDA keeps to monastic rules when it comes to

investigational drugs, meaning any and all statements about the review process come from the companies themselves. In many cases, management's take on the FDA's thinking proves to be out of step with reality. But investors, who have only the companies on which to rely, don't find out until the drug in question gets delayed or outright rejected.

It happened with Axsome Therapeutics, whose treatment for depression appeared on track for approval until last week, when the company disclosed some FDA misgivings that would indefinitely delay the process. Acadia Pharmaceuticals and FibroGen wound up in similar situations earlier this year[18], leaving Wall Street unsure whether to blame an erratic FDA or unreliable CEOs. The cumulative effect is like "our own biotech Delta wave," Evercore ISI analyst Josh Schimmer wrote in a note to clients Saturday.

As for Sesen, Cannell, the CEO, is standing by his positive interpretation of earlier FDA meetings. On Monday, discussing Vicineum's rejection on the conference call, Cannell said the FDA never pointed to any deficiencies in the data from VISTA, never sent the company a disciplinary letter, and said as recently as July that Sesen would not need to run a post-approval trial. Just last Monday, Cannell said, Sesen and the FDA agreed on final wording for Vicineum's label.

"Obviously this is a very surprising turn of events," he said.

Sesen isn't giving up. Assuming the FDA wants data from another pivotal trial, Cannell estimates Sesen would be ready to resubmit Vicineum in 2023. The company has about $150 million in cash, which Cannell said is enough to keep the doors open until then.

As of Tuesday, Sesen was trading at about $1.50 per share.

About the Author

Damian Garde[2]

Damian covers biotech, is a co-writer of The Readout newsletter[19], and a co-host of "The Readout LOUD" podcast[20].

damian.garde@statnews.com [21]
@damiangarde [3]

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